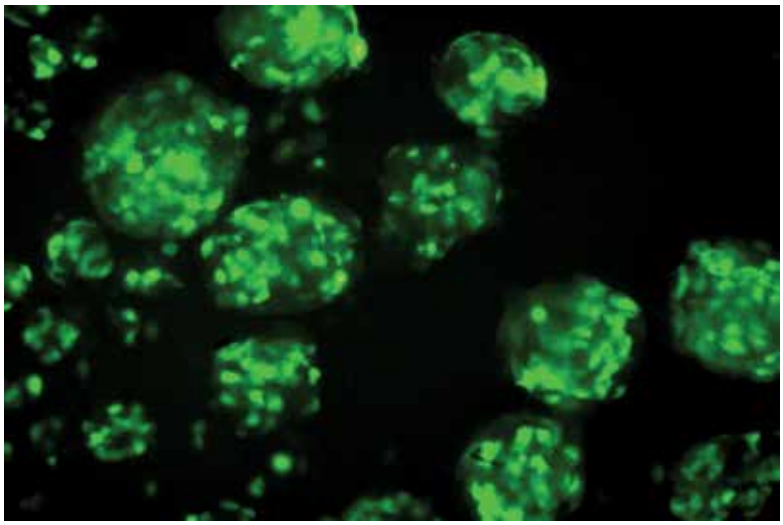
DIVISION OF

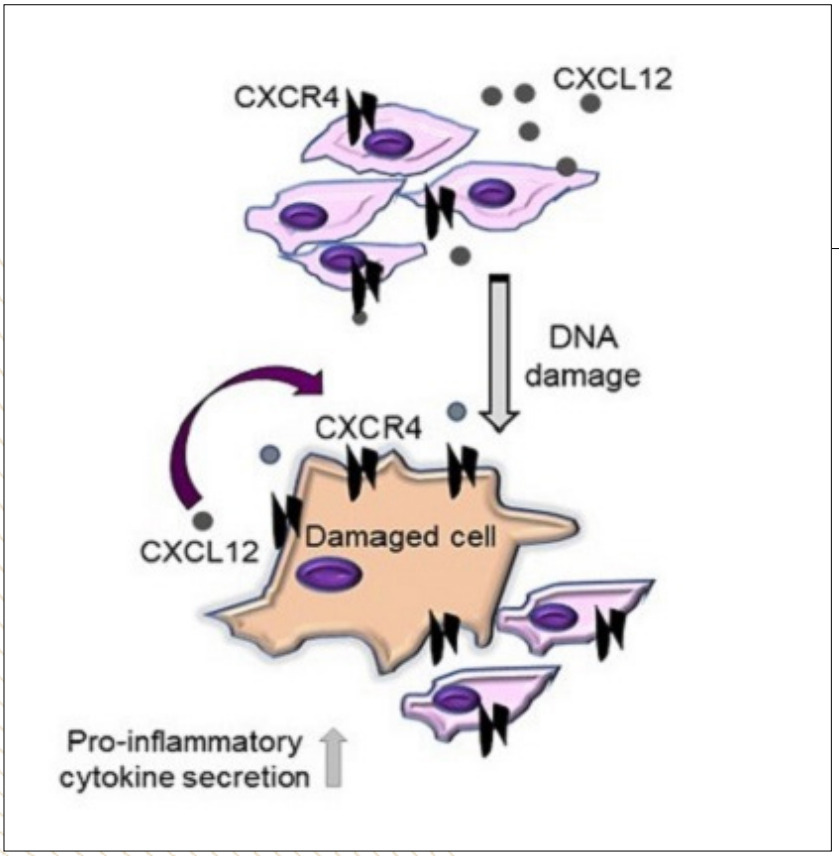
Biological Sciences

RESEARCH SNAPSHOTS 2018



ANNAPOORNI RANGARAJAN (MRDG)

The "stem cell theory" of cancer predicts that cancers originate in the normal, adult stem cells. To test this, Dr. Rangarajan's group introduced various oncogenes into stem/progenitor cells of normal breast tissue cultured as floating 'mammospheres'. A specific "oncogene combination" converted these cells into tumorigenic cells. Interestingly, a significant sub-population of these transformed cells harbored CSCs that initiated new tumors in test animals. Furthermore, gene expression analyses revealed striking similarities between the mammosphere-derived tumors generated within laboratory mice and naturally-arising breast adenocarcinomas encountered in the clinic. This lent early evidence to the provocative notion that solid tumors may originate in adult stem cells. Further, this laboratory-generated breast "cancer stem cell line" also offers a unique system for deciphering the mechanisms of self-renewal in CSCs, and drug-screening.

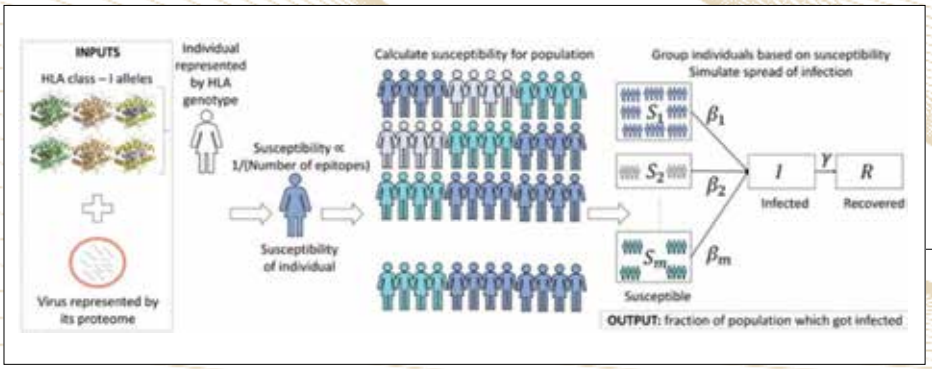


DEEPAK SAINI (MRDG)

Inflammation, characterized by pain, heat and swelling, is the body's response to harmful conditions such as infection and cellular damage. Through inflammation, the body ensures the removal of pathogens, dead cells and regeneration of damaged tissue. However, when the inflammation persists for years permanent tissue damage and even cancer can occur. It has also been found that older individuals have higher levels of inflammation that can persist to chronic levels.

Towards understanding aging and inflammation, Dr. Deepak Saini's lab focuses on a class of receptors known as G protein-coupled receptors (GPCRs) and their roles in the cascade of events which occur when cells grow old aka 'aged'. In a recent study, his group found the mechanism which enhances inflammation when cells undergo DNA damage. Interestingly, they have found that the same mechanism is responsible for increased inflammation during ageing.

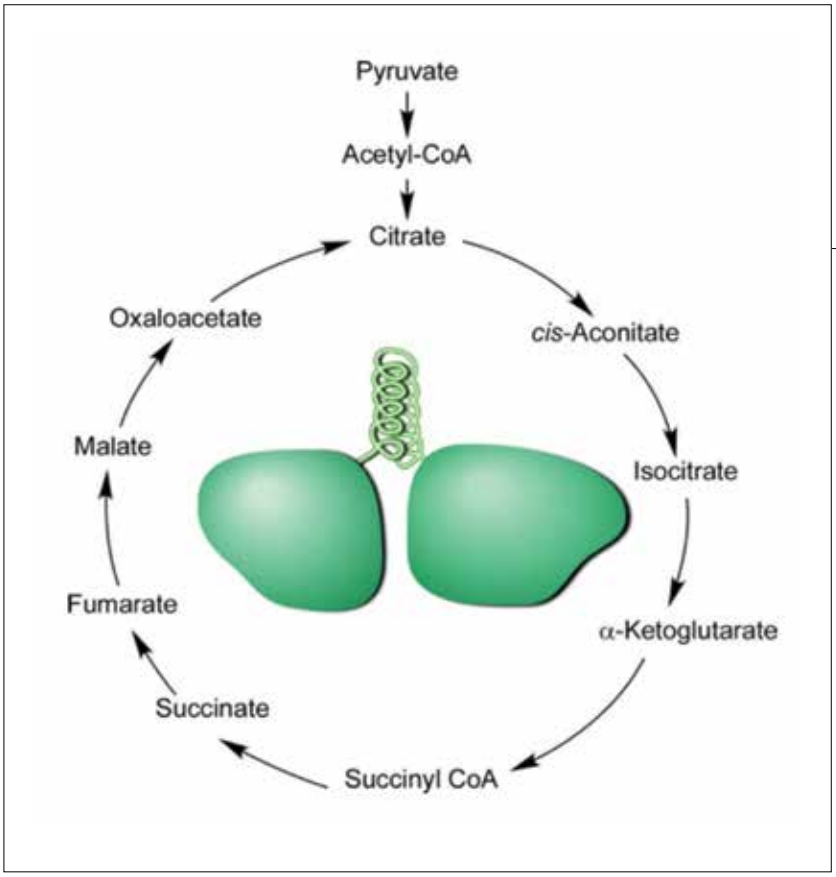
Reference: https://www.nature.com/articles/s41514-018-0028-0 (pdf version)



N CHANDRA (BC)

Levels of immunity to a given strain of H1N1 influenza virus can vary in different people, influencing its spread. Accounting for such variations is a major challenge for the epidemiology of infectious diseases. Real world data is used to estimate susceptibility of individuals in a population, and is a first attempt at understanding how heterogeneity in susceptibility determines disease spread in populations. The results show that larger genetic diversity, leading to the presence of susceptibility sub-populations, protects against the spread of influenza; and populations with a small number of highly susceptible individuals should exhibit smaller outbreaks.

Reference: Sambaturu, Narmada, et al. "Role of genetic heterogeneity in determining the epidemiological severity of H1N1 influenza." PLoS computational biology 14.3 (2018): e1006069.



SANDEEP M ESWARAPPA (BC)

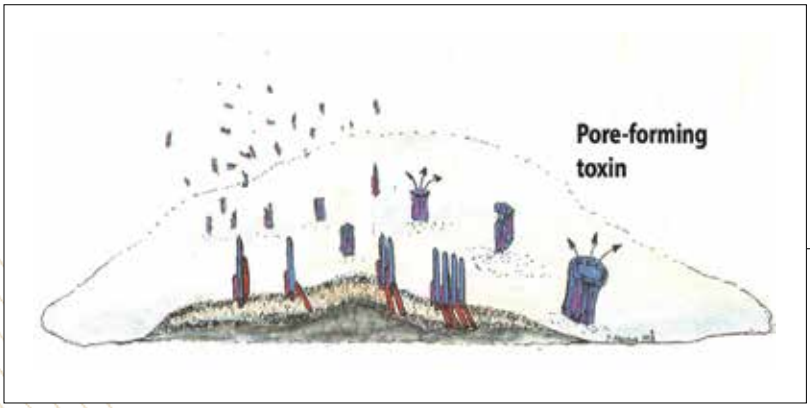
About 1 billion years ago, in a single-celled ancestor of all animals, a gene fusion of two tRNA synthetases formed the bifunctional enzyme, glutamyl-prolyl tRNA synthetase (EPRS). This enzyme ligates amino acids glutamic acid and proline with their cognate tRNAs which is vital for protein synthesis (or translation) in all living organisms. We propose here that a confluence of metabolic, biochemical, and environmental factors contributed to the specific fusion of glutamyl- (ERS) and prolyl- (PRS) tRNA synthetases. To test this idea we developed a mathematical model that centers on the precursor-product relationship of amino acids glutamic acid and proline, as well as metabolic constraints on free glutamic acid availability near the time of the fusion event. Our findings indicate that proline content increased in the proteome during the emergence of animals, thereby increasing demand for free proline.

Reference: Eswarappa SM, Potdar AA, Sahoo S, Sankar S. and Fox PL. (2018) Metabolic origin of the fused aminoacyl tRNA synthetase, glutamyl-prolyl tRNA synthetase. J. Biol. Chem. (in press, Editor's Pick)

SUPRATIM RAY (CNS)

How do the brain signals change when one sees a green jackfruit versus a red tomato? We studied such questions by recording signals from the primary visual cortex of monkeys while they were shown various natural images. To our surprise, we found that there were strong oscillations in the recorded signals at frequencies in the range 30-80 Hz whenever reddish images were shown. These findings provide new insights about the generation of gamma oscillations and processing of colour in the brain.

Reference: Vinay Shirhatti and Supratim Ray (2018). Long-wavelength (reddish) hues induce unusually large gamma oscillations in the primate primary visual cortex. PNAS, April 9, 2018. 201717334; https://doi.org/10.1073/pnas.1717334115



SANDHYA VISWESWARIAH (MRDG), RAHUL ROY (CE), K GANAPATHY AYAPPA (CE)

Certain bacteria produce a class of toxins that poke nanometer-sized holes into animal and human cells. This often results in cells dying. There are a number of steps that occur before a protein forms a pore on a cell membrane. These include binding of the toxin as individual molecules to the membrane, finding other toxin molecules by moving around on the membrane, after which they can start forming ring-like structures by interacting with each other, and finally puncturing a hole in the membrane. An interdisciplinary team from the Centre of Biosystems Science and Engineering, Department of Chemical Engineering and the Department of Molecular Reproduction, Development and Genetics at IISc came together to address this outstanding problem for a pore-forming toxin called Cytolysin A (ClyA) released by the bacteria E. Coli.

References: P. Sathyanarayana, R. Desikan, G. Ayappa and S. S. Visweswariah, "The Solvent-Exposed C-Terminus of the Cytolysin A Pore-Forming Toxin Directs Pore Formation and Channel Function in Membranes", Biochemistry DOI: 10.1021/acs.biochem.6b00593
S Banerjee, S Maurya and R Roy, "Single-molecule fluorescence imaging: generating insights into molecular interactions in virology" J Biosciences, DOI: 10.1007/s12038-018-9769-y
P Sathyanarayana, S Maurya, ABehera, M Ravichandran, SS Visweswariah, KG Ayappa, and R Roy, "Cholesterol promotes Cytolysin A activity by stabilizing the intermediates during pore formation" PNAS (USA), https://doi.org/10.1073/pnas.1721228115

VISHWESHA GUTTAL (CES)

Flocks of starlings, herds of wildebeest, schools of fish, swarms of locusts, colonies of ants, bees and wasps – these examples of sociality are among the most intriguing phenomena in the natural world. It is not surprising, therefore, that the question of why organisms live in groups has attracted a lot of research attention, and today, we have fairly nuanced and in-depth answers to this question. However, our current understanding of sociality comes almost entirely from an intraspecific context, i.e. based on groups of individuals of the same species. We know comparatively little about heterospecific sociality, i.e. social groups or associations among individuals of multiple species.

Hari Sridhar and Vishwesha Guttal from the Centre for Ecological Sciences, survey and synthesise documented examples of heterospecific sociality in the wild, and propose a conceptual framework to understand how organisms decide whether to group with individuals of their own species (conspecifics) or of a different species (heterospecifics).

Reference: Hari Sridhar and Vishwesha Guttal, 2018, Friendship across species borders: factors that facilitate and constrain heterospecific sociality, Phil. Trans. Royal Society of London B, 373: 20170014.

MARIA THAKER (CES)

Wind energy is undoubtedly a safer alternative to fossil fuels, but their ecological consequences are becoming apparent. Over the last few years, we (Maria Thaker from the Centre for Ecological Sciences, and her project students, Amod Zambre and Harshal Bhosale) have been studying the impact of wind-farms on a plateau in the Western Ghats. Like many others, we find that wind farms reduce the abundance of birds, but this has very interesting consequences for the lizards that are their prey. Free of predation pressure, densities of fan-throated lizards were significantly higher in the presence of wind turbines; but their hormonal stress levels, anti-predator behavior, body condition, and even colours were also affected. We conclude that wind-farms have cascading indirect effects on lizards, driven by a combination of predator release and density-dependent competition. These effects are akin to a trophic cascade with wind farms at the top of the food chain.

Reference: Thaker M, Zambre A and Bhosale H. 2018. Wind farms have cascading impacts on ecosystems across trophic levels. Nature Ecology and Evolution. DOI: 10.1038/s41559-018-0707-z